UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,453	08/18/2006	Gina Fischer	028232-0113	3166

22428 7590 01/20/2011

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
01/20/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,453	FISCHER ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *64-66,69-79 and 82-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *64-66,69-79 and 82-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/04/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 11/04/2010 are acknowledged.

2. Claims 80-81 were cancelled. Claims 1-63 and 67-68 had been previously cancelled. Claim 64 was amended.

3. New claims 82-88 were added.

4. Claims 64-66, 69-79 and 82-88 are included in the prosecution.

Information Disclosure Statement

5. The information disclosure statement (IDS) filed on 11/04/2010 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97 and 1.98. Accordingly, the examiner is considering the information disclosure statement. See attached copy of PTO-1449.

Response to Arguments

Rejection of claims under 35 USC § 112

6. In light of the amendment of claim 64 to recite the term "substantially" (with respect to the matrix composition) and to delete "surface active agent" and recite "polyethylene glycol 2000 monostearate or polyethylene glycol 400 monostearate", the rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter) and the rejection under 35 U.S.C. 112, second paragraph, as being indefinite, are withdrawn.

MAINTAINED REJECTIONS:

The following is a list of maintained rejections:

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 64-66 and 79 **remain** rejected and **new claims 82 and 88** are rejected under 35 U.S.C. 103(a) as being unpatentable over Rao et al. (US 2003/0203055 A1).

Rao teaches a method of treating visceral pain (Abstract) and discloses an opioid agonist and morphine (Page 9, [0137]). The active ingredient can be administered orally in solid dosage forms, such as capsules and tablets (Page 12, [0201]). Example 6 discloses a sustained release dosage form containing the active ingredient surrounded by an interior and an exterior wall, with an exit that allows for administration of the active ingredient to a patient (Page 19, [0272]). The sustained release dosage form can include the active ingredient and a polyethylene oxide carrier, which is coated with a wall comprising ethylcellulose (Page 19, [0273]). The sustained release dosage form can also include the active ingredient and a polyethylene oxide carrier, which is coated with an interior wall comprising ethyl cellulose and an exterior wall containing cellulose acetate (Page 19, [0274]). The water insoluble, water impermeable polymeric coating can contain cellulose acetate, ethylcellulose or polyvinyl chloride; and the coating of the tablet can have apertures exposing the core (Page 20, [0285]).

Rao does not expressly teach an example with an opioid in the controlled release polymer matrix that is coated with an insoluble or impermeable coating with apertures.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of treating pain by using an opioid in the sustained release dosage form containing the active ingredient surrounded by a wall, with an exit that allows for administration of the active ingredient to a patient, as suggested by Rao, and produce the instant invention.

One of ordinary skill in the art would do this because analgesics such as opioids are used in the method of treating, as suggested by Rao. It is obvious to substitute one known element (analgesics for pain) for another (opioid for pain) and obtain predictable results. Please see MPEP 2141.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 64, the method of treating a patient suffering from pain that is sensitive to an opioid comprising orally administering such opioid in a controlled release pharmaceutical composition would have been obvious over the method of treating visceral pain (Abstract) by using an opioid agonist or morphine (Page 9, [0137]), as taught by Rao. The limitations of the pharmaceutical composition comprising a matrix comprising polymer(s) and an opioid would have been obvious over the opioid and

morphine (Page 9, [0137]) that may be used in the matrix along with a polyethylene oxide carrier (Page 19, [0273]) as taught by Rao. The limitation of the matrix composition not comprising a surface active agent is obvious over the matrix compositions taught by Rao (Page 19, [0273]). The limitation of the coating that is insoluble in and impermeable to aqueous media is obvious over the wall comprising ethyl cellulose and cellulose acetate (Page 19, [0274]), as taught by Rao. The limitation of the coating having at least one opening exposing at least one surface of the matrix is obvious over the coating of the tablet that can have apertures exposing the core (Page 20, [0285]) as taught by Rao.

Regarding instant claims 65-66, the limitations of the amount of opioid would have been obvious over the method of treating pain (Abstract) by using an opioid agonist or morphine (Page 9, [0137]), as taught by Rao. One of ordinary skill in the art would find it obvious to compare the sustained opioid release with an immediate opioid release in order to determine an efficacious pain treatment regimen. The limitation of measuring the degree of pain would have been obvious as a quantifiable measure of pain treatment that is part of routine experimentation.

Regarding instant claim 79, the limitation of chronic pain would have been obvious over the chronic inflammatory pain taught by Rao (Page 3, [0029]).

Regarding **new claim 82**, the limitation of the polyethylene glycol and polyethylene oxide in the polymer matrix would have been obvious over the polyethylene glycol (Page 12, [0210]) and the polyethylene oxide carrier (Page 19, [0273] - [0274]) taught by Rao.

Regarding **new claim 88**, the limitation of the opioid is obvious over the morphine taught by Rao (Page 9, [0137]).

Response to Arguments

9. Applicant's arguments, see Page 8, filed 11/04/2010, with respect to the rejection of claims 64-66 and 79-81 under 35 U.S.C. 103(a) as being unpatentable over Rao et al. (US 2003/0203055 A1) have been fully considered but are not persuasive.

Applicant argues that: "Rao does not teach or suggest the recited compositions. Moreover, the composition disclosed in Rao has a different structure and mechanism of drug release than the recited compositions. Thus, it would not lead the skilled artisan to the claimed methods." Applicant argues that: "Nowhere does Rao teach or suggest a composition in which the coating layer surrounding the active ingredient-carrier mixture has two openings as claimed. Moreover, Rao does not teach the release of the active agent from the disclosed composition to occur by erosion of the matrix surface as claimed. Rather, release of the active agent from Rao's composition occurs by osmotic pump action."

Applicant argues that: "In sharp contrast, the claimed compositions have two openings in the coat surrounding the matrix. As described in the specification and recited in the claims, the recited compositions achieve controlled drug release by erosion of the matrix, such as by the aqueous biological milieu. Thus, not only do the inventive compositions differ structurally from the composition disclosed in Rao, but they also differ in the underlying mechanism by which controlled release of drug is achieved."

These arguments are not persuasive because the structure (components and arrangement) of the composition, the sustained release from the composition, and a method for treating visceral pain are all taught by Rao. The sustained release dosage form can include the active ingredient and a polyethylene oxide carrier, which is coated with a wall comprising ethylcellulose (Page 19, [0273]). The sustained release dosage form can also include the active ingredient and a polyethylene oxide carrier, which is coated with an interior wall comprising ethyl cellulose and an exterior wall containing cellulose acetate (Page 19, [0274]). Moreover, Rao suggests more than one opening, because of the disclosure that the coating of the tablet can have "**a plurality of formed apertures**" exposing the core (emphasis added, Page 20, [0285]).

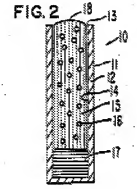
Therefore, the rejection of 08/05/2010 is maintained.

Claim Rejections - 35 USC § 103

10. Claims 64-66 and 79 **remain** rejected and **new claims 82-88** are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al. (US 4,824,675) in view of Rao et al. (US 2003/0203055 A1).

Wong teaches an orally administrable delivery dispenser that contains a drug core with a cellulose acetate wall, a matrix containing tiny pills of the drug and polyethylene oxide, and a mouth in the outer wall (Example 7, Col. 22, line 30 to Col. 23, line 22). The wall forming materials include cellulose acetate (Col. 8, line 39) – which is substantially impermeable to the passage of the drug (Col. 15, lines 32-34), ethyl cellulose (Col. 8, line 64), polyamides (Col. 9, line 1), ethylene-vinyl acetate, polyethylene, ethyl cellulose, and polypropylene (Col. 15, lines 55-63). Matrix

components such as polyethylene oxide (Col. 11, lines 28-29), polyglycolic acid (Col. 13, lines 42-43), polylactic acid (Col. 13, line 45) and polylactideglycolide (Col. 13, line 49) are disclosed. The active drug can be an analgesic (Col. 16, lines 46-48). The following illustrates the arrangement of the inner lumen (14) (or polymeric matrix with the tiny drug-containing pills), the outer wall (12) and the mouth or opening (13).



Wong does not expressly teach an opioid.

The teaching of Rao is stated above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the orally administrable delivery dispenser that contains a matrix containing polyethylene oxide and tiny pills of a drug, where the matrix is surrounded by a cellulose acetate wall, and there is a mouth in the wall, for delivering an analgesic, as taught by Wong, use an opioid as the analgesic in a sustained release dosage form containing the active ingredient surrounded by a wall, with an exit that allows for administration of the active ingredient to a patient, as suggested by Rao, and produce the instant invention.

One of ordinary skill in the art would do this because both Wong and Rao teach the delivery of an analgesic from a sustained release delivery device that contains an inner matrix comprising a polymer and the active, a wall surrounding the matrix formed of impermeable materials, and having an opening or exit in the wall. One of ordinary skill in the art knows that analgesics are used in the method of treating pain and that opioids are used for treating pain, as evidenced by Rao. It is obvious to substitute one known element (analgesics for pain – taught by Wong) for another (opioid for pain – taught by Rao) and obtain predictable results. Please see MPEP 2141.

Regarding instant claim 64, the method of treating a patient suffering from pain that is sensitive to an opioid comprising orally administering such opioid in a controlled release pharmaceutical composition would have been obvious over the orally administrable delivery dispenser that contains a drug core (Example 7, Col. 22, line 30 to Col. 23, line 22) and where the drug can be an analgesic (Col. 16, lines 46-48) as taught by Wong in view of the method of treating visceral pain (Abstract) by using an opioid agonist or morphine (Page 9, [0137]), as taught by Rao. The limitations of the pharmaceutical composition comprising a matrix comprising polymer(s) and an opioid would have been obvious over the delivery dispenser that contains a matrix containing tiny pills of the drug and polyethylene oxide (Example 7, Col. 22, line 30 to Col. 23, line 22) as taught by Wong, in view of the opioid and morphine (Page 9, [0137]) that may be used in the matrix along with a polyethylene oxide carrier (Page 19, [0273]) as taught by Rao. The limitation of the matrix composition not comprising a surface active agent is obvious over the matrix compositions taught by Wong (Col. 22, Example 7) and Rao

(Page 19, [0273]). The limitation of the coating that is insoluble in and impermeable to aqueous media is obvious over the wall forming materials including cellulose acetate (Col. 8, line 39) – which is substantially impermeable to the passage of the drug (Col. 15, lines 32-34), ethyl cellulose (Col. 8, line 64), polyamides (Col. 9, line 1), ethylene-vinyl acetate, polyethylene, ethyl cellulose, and polypropylene (Col. 15, lines 55-63), as taught by Wong and by the wall comprising ethyl cellulose and cellulose acetate (Page 19, [0274]), as taught by Rao. The limitation of the coating having at least one opening exposing at least one surface of the matrix is obvious over the mouth in the outer wall (Example 7, Col. 22, line 30 to Col. 23, line 22 and Fig. 2) as taught by Wong and over the coating of the tablet that can have apertures exposing the core (Page 20, [0285]) as taught by Rao.

Regarding instant claims 65-66, the limitations of the amount of opioid would have been obvious over the method of treating pain (Abstract) by using an opioid agonist or morphine (Page 9, [0137]), as taught by Rao. One of ordinary skill in the art would find it obvious to compare the sustained opioid release with an immediate opioid release in order to determine an efficacious pain treatment regimen. The limitation of measuring the degree of pain would have been obvious as a quantifiable measure of pain treatment that is part of routine experimentation.

Regarding instant claim 79, the limitation of chronic pain would have been obvious over the chronic inflammatory pain taught by Rao (Page 3, [0029]).

Regarding new claim 82, the limitation of the polyethylene glycol and polyethylene oxide in the polymer matrix would have been obvious over the matrix

components such as polyethylene oxide (Col. 11, lines 28-29) taught by Wong and over the polyethylene glycol (Page 12, [0210]) and the polyethylene oxide carrier (Page 19, [0273] - [0274]) taught by Rao.

Regarding new claims 83-87, the limitation of the molecular weight of the polyethylene glycol and polyethylene oxide or block copolymer is obvious over the matrix components such as polyethylene oxide, Polyox ®, having a molecular weight of 100,000 to 5,000,000, as taught by Wong (Col. 11, lines 28-29).

Regarding **new claim 88**, the limitation of the opioid is obvious over the morphine taught by Rao (Page 9, [0137]).

Response to Arguments

11. Applicant's arguments, see Page 9, filed 11/04/2010, with respect to the rejection of claims 64-66 and 79-81 under 35 U.S.C. 103(a) as being unpatentable over Wong et al. (US 4,824,675) in view of Rao et al. (US 2003/0203055 A1) have been fully considered but are not persuasive.

Applicant argues that: "... Wong's wall is separate from its tiny pills, not a coating that is applied to the pills. Thus, the disclosed wall does not read and in no way relates to the recited coating. The Office cites Example 7 of Wong in support of the section 103 rejection, but this embodiment of Wong in no way suggests the claimed invention. The tiny pills of Example 7 are comprised of an active agent core surrounded by cellulose acetate. The pill does not include any type of matrix, let alone a matrix as recited here. The tiny pills are then immersed in a matrix comprising cellulose acetate, polyethylene oxide and hydroxypropylmethyl cellulose. See Wong at column 22, lines 37-39. The pill-

containing matrix is then provided with a wall that comprises cellulose acetate. Thus, the cited example discloses an outer wall surrounding a matrix that has dispersed therein tiny pills comprised of a drug (only) core provided with a cellulose acetate coating. This is a far cry from Applicant's coated matrix compositions. Moreover, Wong's dispenser has a single opening (mouth 13), whereas the instant claims recite compositions comprising a coated matrix, wherein the coating has two openings. In summary, the device disclosed in Wong has a different structure and mechanism of drug release than the recited compositions. Thus, it would not lead the skilled artisan to the claimed methods."

This is not persuasive because the wall (12) as taught by Wong can comprise a semipermeable composition and is nontoxic (Col. 5, line 59 to Col. 6, line 4).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case Wong is combined with Rao.

Rao teaches the structure and arrangement of the components of the composition, along with a method of treating visceral pain. Moreover, Rao suggests more than one opening, because of the disclosure that the coating of the tablet can have "**a plurality of formed apertures**" exposing the core (emphasis added, Page 20, [0285]).

Rao and Wong are properly combined because both Wong and Rao teach the delivery of an analgesic from a sustained release delivery device that contains an inner matrix comprising a polymer and the active, a wall surrounding the matrix formed of impermeable materials, and having an opening or exit in the wall. One of ordinary skill in the art knows that analgesics are used in the method of treating pain and that opioids are used for treating pain, as evidenced by Rao. It is obvious to substitute one known element (analgesics for pain – taught by Wong) for another (opioid for pain – taught by Rao) and obtain predictable results. Please see MPEP 2141.

All the claimed elements are found in Wong and Rao and one with ordinary skill in the art could have combined the elements and the combination would have yielded predictable results. See *KSR International Co. v. Teleflex Inc.*, 550 U.S. - , 82 USPQ2d 1385 (2007).

Therefore, the rejection of 08/05/2010 is maintained.

Claim Rejections - 35 USC § 103

12. Claims 64-66 and 79 **remain** rejected and **new claims 82 and 88** are rejected under 35 U.S.C. 103(a) as being unpatentable over DePrince et al. (US 4,898,733) in view of Rao et al. (US 2003/0203055 A1).

DePrince teaches a method of administering a beneficial agent through oral ingestion of a device (Col. 2, lines 30-34). The beneficial agent can be an analgesic drug (Col. 4, lines 31-40). The device is a compression molded tablet comprising at least two layers; a non-body fluid contacting layer which is sandwiched between two-

body fluid-contacting layers, and the device is partially overlaid with an impermeable coating (Col. 2, lines 35-45, lines 54-64, and Figures 1-2).

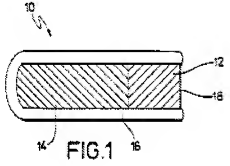
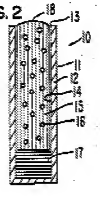


FIG.1

The polymeric material used to form the matrix includes polyethylene glycol (Col. 5, lines 28-35). The tablet is partially coated with a coating material that is impermeable to body fluids and to the beneficial agent and substantially insoluble in body fluids, the sleeve (or coating) may be open at one end, and suitable sleeve materials include cellulose acetate, polyvinyl acetate, polyurethane, polyamide and ethylene-vinyl acetate (Col. 5, line 44 to Col. 6, line 13). The device may then be orally ingested for the continuous administration of the beneficial drug (Col. 6, lines 13-16).

FIG. 2



DePrince does not expressly teach an opioid.

The teaching of Rao is stated above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the orally ingestible device that contains a matrix containing polyethylene glycol and a drug such as an analgesic, where the matrix is surrounded by a coating that is substantially insoluble and impermeable comprising coating materials, and with an opening in the coating, as taught by DePrince, use an opioid as the analgesic in a sustained release dosage form containing the active ingredient surrounded by a wall, with an exit that allows for administration of the active ingredient to a patient, as suggested by Rao, and produce the instant invention.

One of ordinary skill in the art would do this because both DePrince and Rao teach the delivery of an analgesic from a sustained release delivery device that contains an inner matrix comprising a polymer and the active, a wall surrounding the matrix formed of impermeable materials, and having an opening or exit in the wall. One of ordinary skill in the art knows that analgesics are used in the method of treating pain and that opioids are used for treating pain, as evidenced by Rao. It is obvious to substitute one known element (analgesics for pain – taught by Wong) for another (opioid for pain – taught by Rao) and obtain predictable results. Please see MPEP 2141.

Regarding instant claim 64, the method of treating a patient suffering from pain that is sensitive to an opioid comprising orally administering such opioid in a controlled release pharmaceutical composition would have been obvious over the orally ingestible device comprising a beneficial drug such as an analgesic overlaid with an impermeable

coating (Col. 2, lines 35-45, lines 54-64, and Figures 1-2) as taught by DePrince, in view of the method of treating pain (Abstract) by using an opioid agonist or morphine (Page 9, [0137]), as taught by Rao. The limitations of the pharmaceutical composition comprising a matrix comprising polymer(s) and an opioid would have been obvious over the delivery dispenser that contains a matrix containing the drug and polyethylene glycol (Col. 5, lines 28-35) as taught by DePrince, in view of the opioid and morphine (Page 9, [0137]) that may be used in the matrix along with a polyethylene oxide carrier (Page 19, [0273]) as taught by Rao. The limitation of the matrix composition not comprising a surface active agent is obvious over the matrix compositions taught by DePrince (Col. 5, lines 28-35) and Rao (Page 19, [0273]). The limitation of the coating that is insoluble in and impermeable to aqueous media is obvious over the wall forming materials including cellulose acetate, polyvinyl acetate, polyurethane, polyamide and ethylene-vinyl acetate (Col. 5, line 44 to Col. 6, line 13) taught by DePrince and by the wall comprising ethyl cellulose and cellulose acetate (Page 19, [0274]), as taught by Rao. The limitation of the coating having at least one opening exposing at least one surface of the matrix is obvious over the sleeve (or coating) that may be open at one end (Col. 5, lines 62-67) and over the coating of the tablet that can have apertures exposing the core (Page 20, [0285]) as taught by Rao.

Regarding instant claims 65-66, the limitations of the amount of opioid would have been obvious over the method of treating pain (Abstract) by using an opioid agonist or morphine (Page 9, [0137]), as taught by Rao. One of ordinary skill in the art would find it obvious to compare the sustained opioid release with an immediate opioid

release in order to determine an efficacious pain treatment regimen. The limitation of measuring the degree of pain would have been obvious as a quantifiable measure of pain treatment that is part of routine experimentation.

Regarding instant claim 79, the limitation of chronic pain would have been obvious over the chronic inflammatory pain taught by Rao (Page 3, [0029]).

Regarding **new claim 82**, the limitation of the polyethylene glycol and polyethylene oxide in the polymer matrix would have been obvious over the polyethylene glycol (Page 12, [0210]) and the polyethylene oxide carrier (Page 19, [0273] - [0274]) taught by Rao.

Regarding **new claim 88**, the limitation of the opioid is obvious over the morphine taught by Rao (Page 9, [0137]).

Response to Arguments

13. Applicant's arguments, see Page 10, filed 11/04/2010, with respect to the rejection of claims 64-66 and 79-81 under 35 U.S.C. 103(a) as being unpatentable over DePrince et al. (US 4,898,733) in view of Rao et al. (US 2003/0203055 A1) have been fully considered but are not persuasive.

Applicant argues that: "DePrince's three layered system does not teach or suggest the claimed composition comprising an active agent matrix surrounded by a coating layer. That is, the disclosed device does not structurally read on the claimed compositions."

This is not persuasive because DePrince is combined with Rao and the combination of these references renders the structural limitations with the arrangement of the components (matrix, coating, openings) obvious.

Applicant argues that: "The differences between the claimed compositions and those of DePrince are underscored by their different deliver[y] profiles. For example, DePrince's composition does not exhibit zero order release. Moreover, as illustrated in Figure 4, only 75% drug is released after a 35 day study period. Combining Rao with DePrince does not remedy the deficiencies of DePrince, for the reasons set forth above. That is, neither DePrince nor Rao teach or suggest a composition as claimed. Thus, the combination of DePrince and Rao does not support a prima facie case of obviousness."

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., zero order release) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

All the claimed elements are found in DePrince and Rao and one with ordinary skill in the art could have combined the elements and the combination would have yielded predictable results. See *KSR International Co. v. Teleflex Inc.*, 550 U.S. - , 82 USPQ2d 1385 (2007).

Therefore, the rejection of 08/05/2010 is maintained.

Claim Rejections - 35 USC § 103

14. Claims 69-78 **remain** rejected under 35 U.S.C. 103(a) as being unpatentable over Rao et al. (US 2003/0203055 A1) in view of Sackler et al. (US 5,478,577).

The teaching of Rao is stated above.

Rao does not expressly teach the mean plasma concentration of the opioid or a once daily administration of the opioid.

Sackler teaches a method for providing effective pain management in humans for a time period of about 24 hours, comprising preparing a solid, controlled-release oral dosage form by incorporating an analgesically effective amount of an opioid analgesic into a controlled release dosage form which provides a rapid rate of initial rise of the plasma concentration of the opioid such that the peak plasma level of the opioid analgesic obtained in-vivo occurs from about 2 to about 8 hours after administration of the dosage form (Col. 4, lines 3-14). Sackler teaches that the oral opioid analgesics have been formulated to provide for an increased duration of analgesic action allowing once-daily dosing (Col. 7, lines 52-54). Morphine sulfate is used at 30mg dosage (Col. 13, line 44 to Col. 14, line 8, Table 1, Examples 1-2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use an opioid as the analgesic in a sustained release dosage form containing the active ingredient surrounded by a wall, with an exit that allows for administration of the active ingredient to a patient, as suggested by Rao, in view of the oral once daily administration of an opioid with a plasma concentration of the opioid such that the peak plasma level of the opioid obtained in-vivo occurs from about 2 to

about 8 hours after administration of the dosage form, as suggested by Sackler, and produce the instant invention.

One of ordinary skill in the art would do this because determination of the plasma concentration of the opioid formulation is part of routine experimentation when orally administering opioids for the treatment of pain.

Regarding claims 69-75, the recitations of the plasma concentration over various time periods would have been obvious variants over the sustained release orally administrable dosage forms taught by Rao (Page 19, [0272] – [0274]), and Sackler (Col. 7, lines 52-54) and the plasma concentrations taught by Sackler (Col. 4, lines 3-14) unless there is evidence of criticality or unexpected results.

Regarding claims 76-77, the limitation of once daily administration of the composition would have been obvious over the once-daily dosing taught by Sackler (Col. 7, lines 52-54).

Regarding claim 78, the limitation of 15 to 300 mg of morphine sulphate would have been obvious over the morphine sulfate used at 30mg dosage as taught by Sackler (Col. 13, line 44 to Col. 14, line 8, Table 1, Examples 1-2).

Response to Arguments

15. Applicant's arguments, see Page 11, filed 11/04/2010, with respect to the rejection of claims 69-78 under 35 U.S.C. 103(a) as being unpatentable over Rao et al. (US 2003/0203055 A1) in view of Sackler et al. (US 5,478,577) have been fully considered but are not persuasive.

Applicant argues that: "While Sackler teaches that certain drug delivery profiles may be desirable, it does not teach or suggest that the disclosed delivery profiles could be achieved using Rao's composition. Thus, there is no rational basis for the obviousness rejection."

This is not persuasive because one of ordinary skill in the art would find it obvious to use an opioid as the analgesic in a sustained release dosage form containing the active ingredient surrounded by a wall, with an exit that allows for administration of the active ingredient to a patient, as suggested by Rao, in view of the method for providing effective pain management in humans for a time period of about 24 hours, as taught by Sackler, because both references are drawn to methods of treating pain with an opioid analgesic. One of ordinary skill in the art would do this because determination of the maximum plasma concentration of the opioid formulation over different periods of time is part of routine experimentation when orally administering opioids for the treatment of pain. The recitation of the mean maximal concentration obtained by the dose over different periods of time is an obvious variant.

Therefore, the rejection of 08/05/2010 is maintained.

Conclusion

16. No claims are allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/Humera N. Sheikh/
Primary Examiner, Art Unit 1615